Pericardial Disease

Introduction: Conundrums and Challenges Regarding the Pericardium

The pericardium is a structure that appears grey on ultrasound (echocardiogram) and marks the outer boundary of the middle inferior mediastinum. There is one pericardium, and it is the **fibrous pericardium**. The fibrous pericardium is distensible—not as stiff as cartilage, but far stiffer than connective tissue that carries blood vessels, lymphatics, and nerves—and acts as a barrier for the heart and its pericardial cavity. The **pericardial cavity** is fluid-filled and identified on echocardiogram as a small, black rim of fluid that separates the myocardium from the fibrous pericardium. You are starting with the correct perspective. There are three things: fibrous pericardium, pericardial cavity with fluid in it, and heart.

There are NOT "three layers of the pericardium." There is NOT a serous pericardium and a fibrous pericardium. The reason that so many people, resources, and educators state that there are three layers of the pericardium, namely—two layers of serous and one layer of fibrous pericardium—is because the concept of a Body Cavity is relatively new (the capitalized Body Cavity, a fluid-filled sac lined with mesothelium, coined by Dr. Williams). The myocardium of the heart has its connective tissue with blood vessels, lymphatics, and nerves—the epicardium. The fibrous pericardium has its connective tissue with blood vessels, lymphatics, and nerves. But that connective tissue doesn't have a special name because it is the adventitia of the rest of the mediastinum. Between the fibrous pericardium and the epicardium is the pericardial cavity, a Body Cavity.

Because a Body Cavity cannot be held in the hands or seen with a microscope, when medical science first started looking at the heart (the heart alone, not a cross-section of the heart plus the fibrous pericardium) on a flat slide, it saw myocardium, then epicardium, then mesothelium. That lining of mesothelium really belongs to the pericardial cavity. But because the rest of the cavity wasn't there, medical science assumed that this mesothelium belonged to the heart. So was it decreed: *the epicardium is lined with the visceral pericardium*. When today's medical scientists mention epicardium, sometimes they mean the connective tissue, and sometimes they mean the epicardium with the visceral pericardium. Then, when medical science looked at the fibrous pericardium under a microscope, they saw the organ and its connective tissue, which also ended with mesothelium. That lining of mesothelium also really belongs to the pericardial cavity. But because the rest of the cavity wasn't there, medical science assumed that this mesothelium belonged to the fibrous pericardium. Thus was it written: *there is a parietal pericardium*. But hang on, we know there is a pericardial cavity and that it has serous fluid in it. This would mean that the order is: the visceral serous pericardium, the parietal serous pericardium, and the fibrous pericardium. Now we've got it! And the falsehood is perpetuated again and again: there are "three layers of pericardium: fibrous, parietal serous, visceral serous."

What compounds this misunderstanding is that it doesn't matter to a surgeon taking care of a patient with fibrinous pericarditis after a CABG. Although the thin rim of black on the echocardiogram does confirm the positioning of the echo, when the chest is cracked open for heart surgery, the surgical pericardium—the connective tissue, fibrous pericardium, and pericardial cavity—is less than one centimeter thick combined. The scalpel goes through the pericardium, and the surgeon is at the heart. The surgeon cannot even appreciate the simple mesothelium. So although it is true that it doesn't have much significance in practice, it has much significance for a new learner. Rather than memorize and regurgitate, start with understanding, and you can focus on getting to clinical practice faster.

The **pericardial cavity** is NOT a *potential* space, as many claim it to be. It is a Body Cavity, a fluid-filled space lined with mesothelium. It enables the heart to remain near but separate from the fibrous pericardium, the fluid within the pericardial cavity preventing the mesothelium from touching and fusing. If the pericardial cavity had no fluid in it, the two surfaces would become adherent, the

epicardium acting as adventitia to the myocardium and fibrous pericardium. Too much fluid in the pericardial cavity can be problematic, but a little fluid is required so that the fibrous pericardium and the epicardium do not fuse. When they do, it is a pathologic condition discussed in this lesson.

The closeness of the layers introduces further conundrums to the study of this subject. The diagnosis of **pericarditis** does not distinguish the epicardium from the pericardium, even though inflammation of the pericardium causes chest pain because it has somatic nerves, and inflammation of the epicardium causes ST-segment changes because it touches the myocardium. The subtypes are determined by the consistency of the fluid in the pericardial cavity. And sometimes pericarditis isn't even an -itis at all. Histological inflammation means the "presence of immune cells." Some forms of pericarditis will not have any.

SO. What is taught in this lesson are the generally accepted clinical features of pericardial disease. What does that mean? Anything that involves the epicardium, pericardial cavity, or fibrous pericardium, collectively "the Pericardium." From this point forward, Pericardium refers to all three layers and is meant to be nonspecific. If we need to get specific, we'll use the noncapitalized complete name.

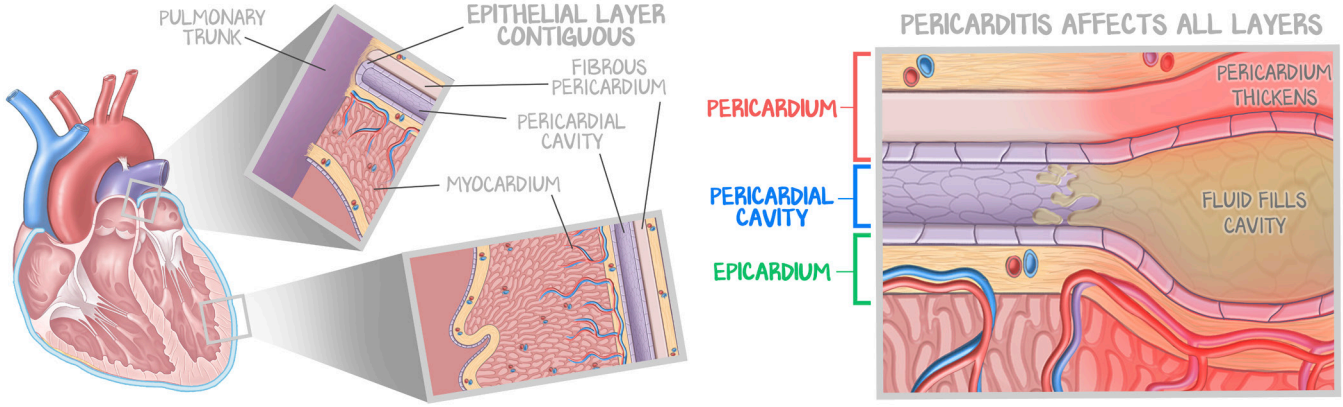

Figure 3.1: Anatomy of the Pericardium and Pericarditis
The fibrous pericardium is the rigid but stretchy container that holds the heart in place. The "serous pericardium" is a Body Cavity, the pericardial cavity. When there is inflammation of the fibrous pericardium, the pericardial cavity can be involved, with immune cells in the Pericardium, pericardial cavity, or both. When there is inflammation of the epicardium, the pericardial cavity can be involved, with immune cells in the epicardium, pericardial cavity, or both. Whether the condition is epicarditis, "pericardial cavititis," or "fibrous pericarditis," medical science makes no distinction. They are all summed as Pericarditis.

Acute Pericarditis

The following are the accepted signs and symptoms of acute pericarditis. Because the epicardium, pericardial cavity, and fibrous pericardium are so close together, inflammation of one is assumed to be inflammation of them all. Therefore, acute pericarditis is inflammation of the pericardium (not capitalized). Inflammation of the pericardium presents with three key features: pleuritic chest pain, pericardial friction rub, and EKG changes.

Pleuritic chest pain. Acute pericarditis presents with a **sharp chest pain** that is both **pleuritic** (worse with inspiration) and **positional** (leaning forward relaxes the pericardium, improving the pain, whereas leaning back stretches it, worsening the pain).

Pericardial friction rub. A pericardial friction rub is a superficial scratchy or squeaky sound best heard at the left sternal border caused by the beating of the heart against inflamed pericardium. It is described as a **continuous murmur** but may have three components, which correspond with atrial systole, ventricular systole, and early diastole. It can be confused with a pleural friction rub, which has a similar

quality and character. Patients can control their breathing, so they can terminate the pleural friction rub by holding their breath. But patients cannot voluntarily pause their heart, so **holding their breath does not eliminate the pericardial friction rub**.

The **EKG findings** in pericarditis are also classically defined. There will be **ST-segment elevation** in **all leads** (indicating that there is no focal myocardial infarction, which would appear with ST-segment elevations in some leads with reciprocal changes in others) and a **depressed PR segment**. These findings are pathognomonic for pericarditis.

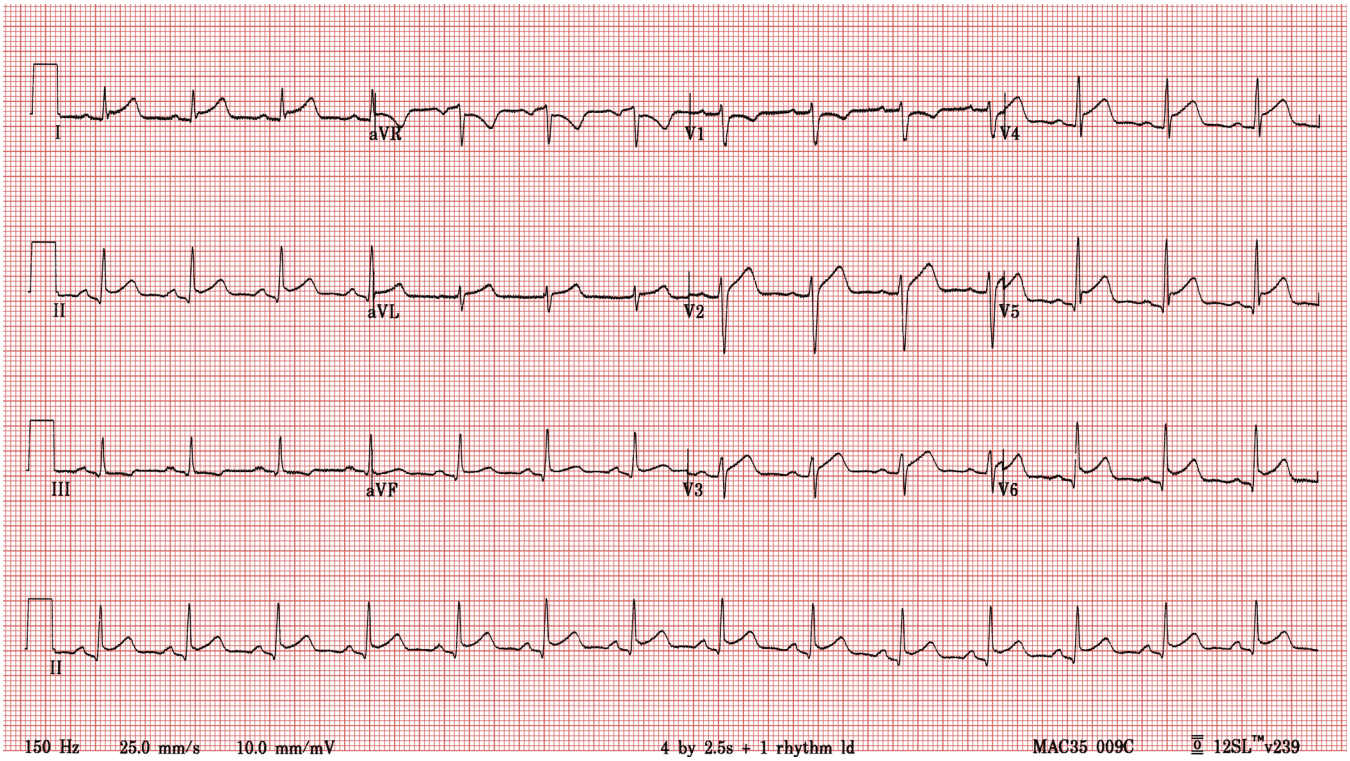

Figure 3.2: EKG of Pericarditis
The pathognomonic finding of acute pericarditis. Although it is only one of four diagnostic criteria, ST-segment elevation in all leads can be no other disease. The depressed PR segment, the lowering of the isoelectric line, gives the appearance of ST-segment elevation when none actually exists. Because it is far easier to recognize diffuse ST-segment elevation, that's how we want you to learn it, leaving the isoelectric line to EP cardiology subspecialists.

Pericarditis is very difficult to visualize with imaging. **No imaging other than an EKG** can diagnose pericarditis. Even an MRI can only reveal suggestive inflammation and is less sensitive than EKG. Imaging can diagnose complications of pericarditis (such as pericardial effusion), but not the inflammation itself.

A laundry list of pericarditis causes only induces learners to abandon any attempt at memorization. This is because pericarditis etiology rarely dictates treatment or disease course. Pericarditis is generally self-limiting and responds very well to anti-inflammatories. However, you do need to be aware of some of the common causes and some of the high-yield ones. The most common cause is **idiopathic**, chalked up to a virus but never confirmed. **Infectious** etiologies are also common, **viral** (coxsackie B) leading in the First World, **TB** in the developing world. **Uremia** is a common cause in those with end-stage renal disease (expect a BUN in the triple digits and altered mentation to go along with the pericarditis). Still other causes are the **serositis of rheumatological disease** (lupus, rheumatoid arthritis). Some rarer causes are **cancers of nearby structures** (e.g., lung, breast, esophagus, lymphoma) or any radiation therapy.

If there is an underlying cause, treat the cause. As most causes are idiopathic (aka viral), empiric treatment is the standard. The **best treatment** is a combination of **both colchicine and NSAIDs**. NSAIDs are limited by renal disease; colchicine is limited by diarrhea. If one can't be given, give the other. If neither can be given, give **prednisone** knowing that glucocorticoids increase the risk of relapse, especially if the etiology is viral. We detail the mechanisms of colchicine and NSAIDs in MSK: Rheumatology #2: *Gout Pharmacology*. For now, memorize "if pericarditis, colchicine and NSAIDs is the best answer."

Acute Pericarditis Subtypes

Although pericardial disease has many causes, the morphological reaction of the Pericardium to injury is rather limited. The Pericardium reacts to acute injury by exuding fluid, fibrin, cells, or a combination thereof. The cause of the pericardial disease determines the type of fluid and/or cells exuded into the pericardial cavity.

Serous pericarditis. When the injured Pericardium produces no fibrinous exudate, and there aren't any cells, the condition is called serous pericarditis. Serous pericarditis is, therefore, a pericardial effusion. YES. "Serous pericarditis" means "makes more serous fluid than normal" because the pericardial fluid is already serous. Producing excess pericardial fluid is also called a pericardial effusion (more on this later). Serous pericarditis is seen in pericarditis caused by **viruses**.

Fibrinous pericarditis. This is the most common type of pericarditis. And be careful, this is pericarditis with a fibrinous exudate in the pericardial cavity, not inflammation of the fibrous pericardium. Fibrin is the primary protein in the fluid in which leukocytes do their work. There isn't an acute inflammatory reaction that is very severe (neutrophils, macrophages, then fibroblasts), so the risk of scarring is low. With repeated attacks of fibrinous pericarditis, scarring is possible. Scarring is constrictive pericarditis, discussed below, what happens when the mesothelium gets smooshed together, and the edges of the pericardial cavity adhere to one another. But deposition of fibrin will be visible on gross examination of the heart (the epicardium will have a fibrin network adhered to it when the pericardial cavity is taken away). Look for **post-infarction fibrinous pericarditis** (**2–4 days** following a nonreperfused myocardial infarction, associated with coagulative necrosis), **post-infarction syndrome** (Dressler syndrome, **2–4 weeks** after a nonreperfused myocardial infarction), trauma, and cardiac surgery.

Purulent/suppurative pericarditis. When caused by an invasion of bacteria, the response to the infection is the same as it is everywhere else—acute inflammation: neutrophils, macrophages, fibroblasts. The presence of **pus in the pericardial fluid** means a bacterial infection (frank pus to the naked eye is a mass of neutrophils under the scope). Purulent pericarditis is extremely difficult to anticipate on first presentation and is only suspected after empiric treatment fails, or pericardial fluid that warrants drainage AND that drainage has pus. Rarely is the suspicion of suppurative pericarditis the cause to go looking at the fluid. Instead, there is a fever that resists treatment, and there happens to be fluid around the heart. The fluid is assessed because no answer can be found. As soon as pus is detected, the diagnosis and management shift. It is hard to get to the pericardial cavity. There is the fibrous pericardium, a shell on the outside protecting the contents of the middle mediastinum from the rest of the mediastinum, and a thick myocardium underneath. To infect the pericardial cavity requires **intrathoracic inoculation** or **hematogenous spread**. That usually means a complication of surgery near the heart or a major infection near the heart. The intense inflammatory response and subsequent scarring frequently produce constrictive pericarditis (see below). **Drainage**, **IV antibiotics**, and even surgery may be required. A more active inflammatory response means more fibroblast activity. Suppurative pericarditis has the greatest likelihood of organizing, leading to adhesions and constrictive pericarditis. "Organizing" means that the fibrinous exudate in which neutrophils and macrophages fought the bacteria becomes infiltrated by fibroblasts and made permanent by the laying down of collagen (explored in greatest detail in Pulmonary: Lung #9: *Pneumonia*).

Constrictive Pericarditis

If you inflame something enough, it will scar. If you inflame two things next to each other, they can sort of meld and scar together. The Pericardium is no different. The fibrous pericardium is made of fibroelastic material. It is supposed to stretch, accommodating the expanding ventricle during diastole. It separates the heart and pericardial cavity from the rest of the mediastinum, but it gives room for the ventricle to relax during diastole. When scarred, it ceases to be elastic and becomes more like concrete. This prevents relaxation of the ventricles and impairs diastolic filling. This mimics the physiology of restrictive cardiomyopathy, and hemodynamically the two diseases are nearly impossible to separate. In constrictive pericarditis, the heart cannot relax because the fibrous scar surrounding it won't let it. In restrictive cardiomyopathy, the heart cannot relax because the myocardium is too thick, filled with something other than myocytes. Either way, no relaxing, no filling. This causes diastolic heart failure that presents with jugular venous distension, peripheral edema, and dyspnea on exertion (more details on heart failure symptoms in Structure and Function #6: *Heart Failure*). Adding venous return to a heart that cannot relax will not help it fill. **Kussmaul's sign** is an **increase in jugular venous pulsation on inspiration** (the opposite of what should happen). The venous return is increased—the inspiration drawing blood to the heart—but the heart cannot accept any more blood, so the blood follows the path of least resistance back up the vena cava. Both restrictive cardiomyopathy and constrictive pericarditis exhibit the same physiology and Kussmaul's sign. How do you tell them apart then?

In constrictive pericarditis, there is a **pericardial knock**, the sound of the ventricle striking its now-rigid cage, and there must be a history of pericarditis. Restrictive cardiomyopathy has no such knock and no history of pericarditis (and often a history of infiltrative disorder affecting another organ besides the heart). Constrictive pericarditis can also result in adhesions, the ventricle stuck to the hard box.

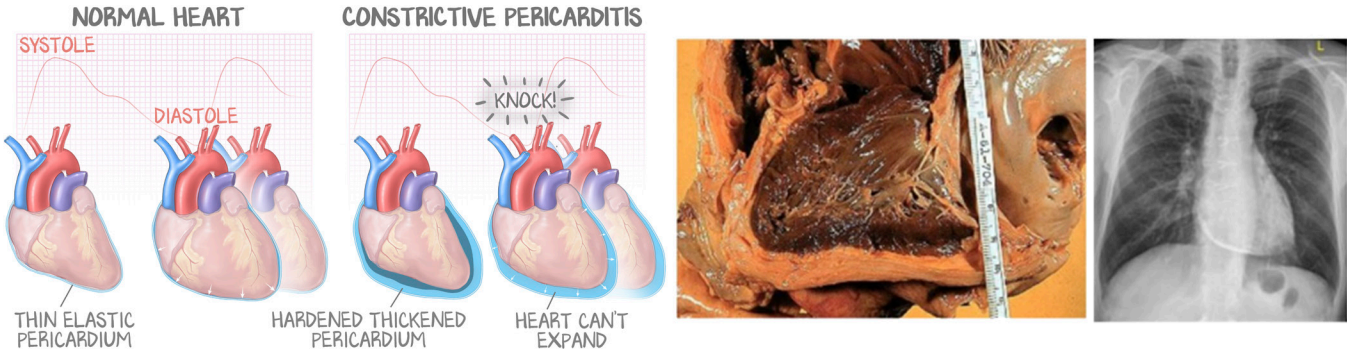

Figure 3.3: Constrictive Pericarditis
In a normal heart, the thin fibroelastic pericardium accommodates the relaxing heart. During systole, the ventricle gets smaller as it ejects blood. During diastole, the ventricle gets larger as it fills with blood. In constrictive pericarditis, the pericardium isn't just thickened but stiffened like concrete and does not stretch to accommodate the expanding ventricle in diastole. A gross sample shows a thickened tan pericardium and a ventricle that is compressed by its shape. The X-ray demonstrates calcification, the white line under the heart representative of the scarred Pericardium.

X-ray of the chest may show calcification of the Pericardium. Echocardiogram cannot confirm the scarring, only rule out an effusion and rule out ventricular hypertrophy. MRI is the best test to confirm constrictive pericarditis. **Pericardiectomy**—surgical excision of the entire Pericardium—is the only treatment.

Pericardial Effusion

There is supposed to be 15–50 mL of pericardial fluid in the pericardial cavity. That gives the heart lubrication to beat comfortably. But too much fluid in the pericardial cavity is called a **pericardial effusion**. Pericardial effusions can be caused by pericarditis, but also by plenty of things that aren't pericarditis. This confuses learners tremendously. You should learn pericarditis as causing chest pain and friction rub, and pericardial effusion as causing **painless dyspnea**. The thing that makes the patient feel pain is inflammation of the pericardium. But think about this now: if the epicardium is inflamed and has no somatic nerves, and there is a big pocket of fluid between the inflamed epicardium and the fibrous pericardium that does have somatic nerves, the inflamed epicardium may not inflame the Pericardium.

Pericarditis can cause effusions. That means there may be the chest pain of pericarditis and pericardial effusions. Effusions can occur without pericarditis. That means there may be a pericardial effusion without chest pain. Keep it easy by separating pericarditis from pericardial effusion.

The accumulation of fluid causes the heart sounds to be more poorly transmitted, as they are now farther away from the chest wall, separated by intervening fluid. That means there will be **diminished heart sounds** and **no friction rub**. The **EKG findings** are not as pathognomonic as for pericarditis but may show **electrical alternans** (alternating of the QRS amplitude) because the heart can move more freely in a larger pocket of fluid. The heart swings near-then-away with each heartbeat, and the movement of the heart is visualized by alternating QRS complexes. Rather than being tethered by the fibrous pericardium, the heart has a bath of low-resistance fluid to move around in, first forward, then back.

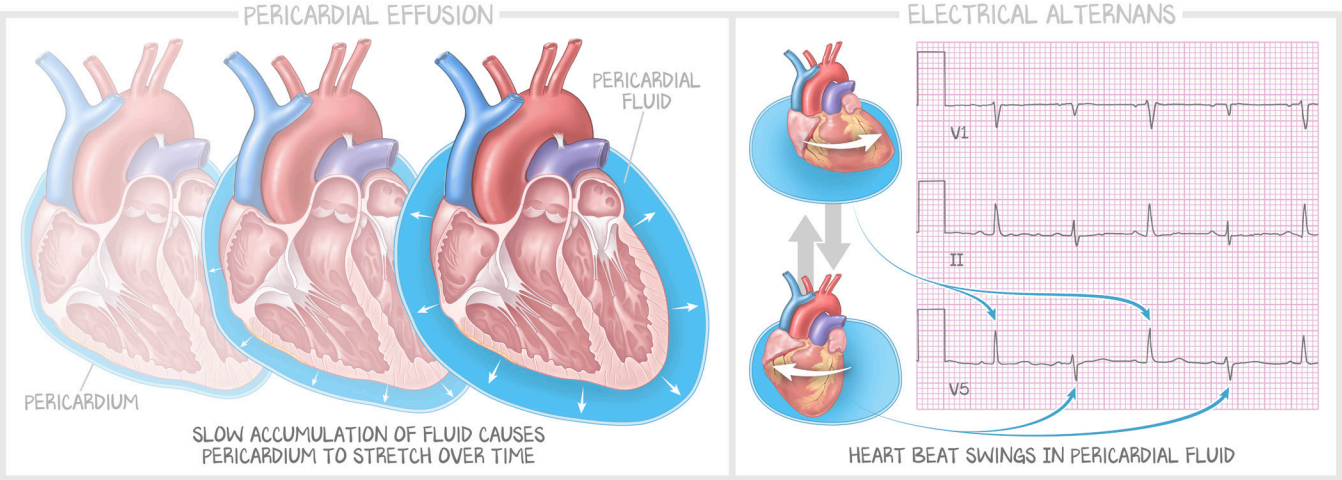

Figure 3.4: Pericardial Effusion
(a) Representation of the accumulation of pericardial fluid. (b) Electrical alternans.

Various imaging modalities can yield the diagnosis. An **X-ray** will show a **water-bottle heart** with what appears to be extreme cardiomegaly. Really, it is the shadow created by the excess fluid. **CT** is not the test of choice for pericardial effusion, but if performed with intravenous contrast, the chambers will light up nicely, whereas the fluid in the pericardium will not. The **best test** for diagnosing a pericardial effusion is an **echocardiogram** (synonymous with a bedside ultrasound), which can easily identify the fluid. You look for the fibrous pericardium (the bright white thing), which should be separated by the grey thing with chambers (the heart), and assess whether there is a smidgen of black between them (a normal amount of fluid) or a lot of black between them (a pericardial effusion). These radiographic tests do nothing to determine etiology but can identify the pocket of fluid.

Imaging cannot help determine the etiology of an effusion. A pericardial effusion is more of a radiographical diagnosis. Pericardial effusions do not require drainage unless recurrent or refractory, or there is tamponade. Usually, the underlying diagnosis is known, and you treat that underlying diagnosis.

Hemorrhagic effusions mean **blood in the space** and occur with dissecting hematomas and post-surgery changes. A **malignant effusion** may be bloody, and cytology will be positive for cancer. An **exudative** effusion is seen in infections (TB, bacterial), as we discussed above (purulent/suppurative pericarditis). Still, there may be a **transudative** effusion due to CHF, myxedema, or nephrotic syndrome. The only way to know is to **tap it**. You should be able to anticipate the findings in the fluid (the person with overwhelming sepsis and an effusion has an infectious effusion), and you should be able to view the findings and anticipate the diagnosis (lots of red blood cells means bleeding).

Pericardial Tamponade

The fibrous pericardium is made of fibroelastic material. It can stretch, but only a little, designed to take the shape of diastolic filling. It also is supposed to have fluid in the pericardial cavity. If given enough time, it will stretch out, conforming to the new larger shape. That means that small pericardial effusions and large pericardial effusions that accumulate slowly over time can be accommodated by the fibrous pericardium. But it does have its limits. Pericardial effusions are pericardial effusions until those limits are reached. Pericardial effusions cause pericardial tamponade when those limits are exceeded, and the pericardial fluid compresses the right ventricle enough to induce hemodynamic consequences.

Pericardial tamponade is pericardial effusion with hemodynamic consequences.

If a pericardial effusion accumulates **rapidly** (so there isn't time for the fibrous pericardium to stretch out) or is a **large volume** (so it doesn't matter whether the fibrous pericardium had time to stretch out), the effusion can **impair ventricular filling**. The heart changes shape when it contracts, getting smaller to expel blood. It is then supposed to relax to fill for the next beat, expanding the ventricular volume. In tamponade, the ventricles contract without difficulty, decreasing their volume. With pericardial pressures so high, the right ventricle, left ventricle, and pericardial effusion are competing for space. So, in tamponade, the effusion takes up the space of that decreased volume, preventing relaxation, and thereby preventing diastolic filling. If the heart can't fill, the heart can't empty.

The clinical presentation of cardiac tamponade is **Beck's triad**: hypotension, jugular venous distension, and distant heart sounds. **Hypotension** because of compromised venous return and impaired cardiac output. **Jugular venous distension** but clear lungs because the right heart is compromised more than the left, and venous return backs up before the broken pump. **Distant heart sounds** because of the effusion.

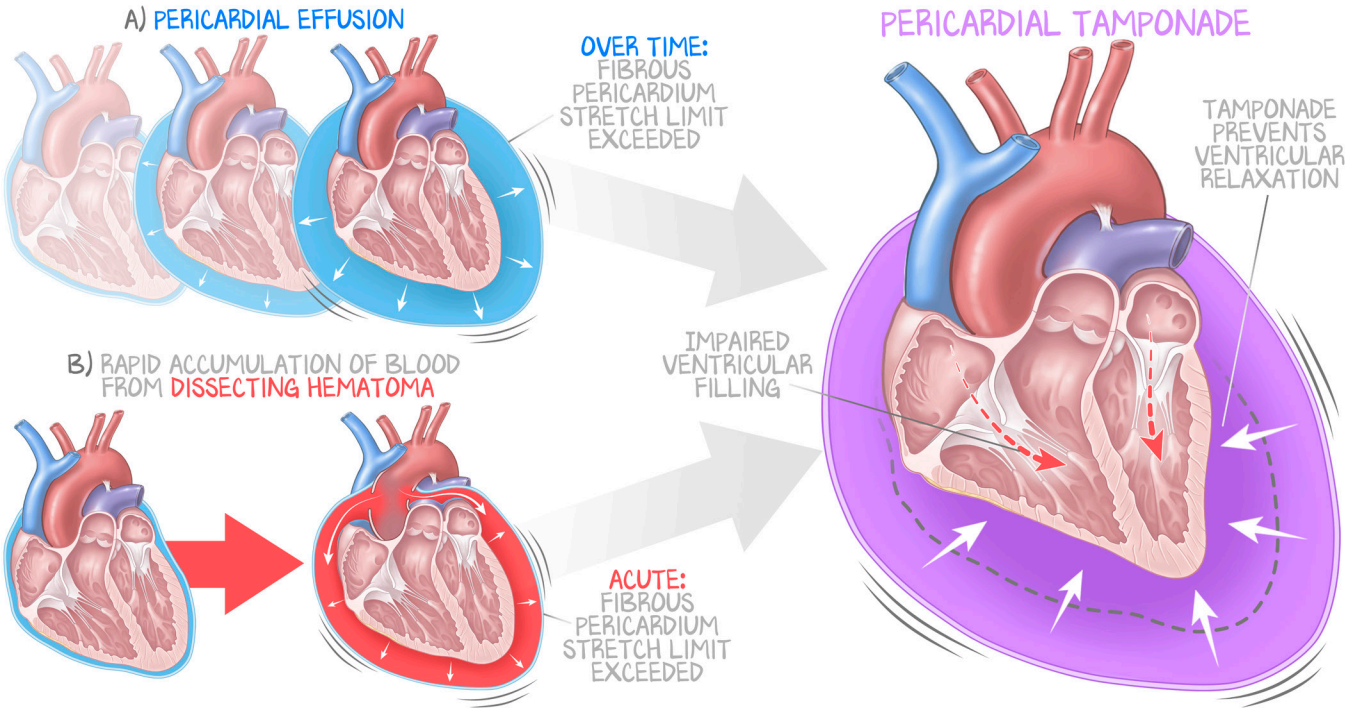

Figure 3.5: Pericardial Tamponade
(a) A slowly developing pericardial effusion gradually stretches the Pericardium. Eventually, even though the change was slow and allowed the Pericardium to accommodate, it reaches its limits and does not accommodate further. Huge effusions can cause tamponade this way. (b) Smaller pericardial effusions can also cause tamponade, especially when the accumulation is rapid, such as when an aortic dissection causes hemorrhage into the pericardial cavity.

The diagnosis of pericardial tamponade is not made with any imaging or EKGs. The diagnosis is made with a **physical exam maneuver—pulsus paradoxus**. Pulsus paradoxus is a normal phenomenon whereby inspiration causes increased venous return to the right heart. Generated by negative intrathoracic pressure, blood is pulled from the veins into the right heart. The right chambers are more filled with blood, which means a larger volume. This larger volume sort of nudges over to the left chambers, limiting their size, which means limiting their volume. On the next contraction—less blood into the left heart, less blood out—there is a slightly lower stroke volume and, therefore, slightly lower systolic blood pressure. The reverse happens on exhalation. The right chambers see less venous return and so are smaller in volume. But also, the sequestered blood in the pulmonary veins isn't sequestered, and the increased volume of blood just ejected by the right ventricle during inhalation is now translated as an increased venous return to the left. Thus the variation in systolic blood pressure can be up to 10 mmHg (but is usually < 5 mmHg) between inhale and exhale.

In cardiac tamponade, pulsus paradoxus is exaggerated. There just isn't enough room for both ventricles, so they compete for space. During inhalation, the right ventricle receives more preload, more venous return. This **increases the right ventricular volume**. But because there is no extra room in the pericardial space to expand into, the **right ventricle expands into the left ventricle**. This means a smaller left ventricle, which means a smaller end-diastolic volume for the left ventricle, which in turn means less stroke volume and, therefore, cardiac output on the left heart's next beat. That "being nudged by" the right ventricle happens normally, as described in the last paragraph. But then there is an **additional compromise of the left ventricular venous return** caused by the **bowing of the right ventricle into the left**. Therefore, the finding of **exaggerated pulsus paradoxus**, a change in systolic blood pressure **> 10 mmHg** (a decrease of 10 points) defines the hemodynamic consequence of tamponade, and the diagnosis is made.

An echocardiogram can demonstrate septal bowing. It can show you a big effusion. Tamponade is a clinical diagnosis made by identifying the hemodynamic changes on vital signs, not on radiographs. In truth? If someone is hypotensive with jugular venous distension and muffled heart sounds, you won't take the time to perform pulsus paradoxus. You'll be too busy finding the pericardiocentesis needle and turning on your ultrasound (or at least calling cardiology).

If you diagnose pericardial tamponade, the correct answer is to relieve the pressure with **pericardiocentesis**, drainage of the fluid by shoving a needle under the person's rib cage. Open surgical drainage or **pericardial window** is usually reserved for patients already in the operating room or those with a recurrent or refractory effusion. If you do not have a pericardiocentesis tray at the bedside, **give a bolus of intravenous fluids**. This increase in venous return will initially support the filling of the ventricles, temporizing the patient. If you are asked to choose between options, drainage is the right answer.

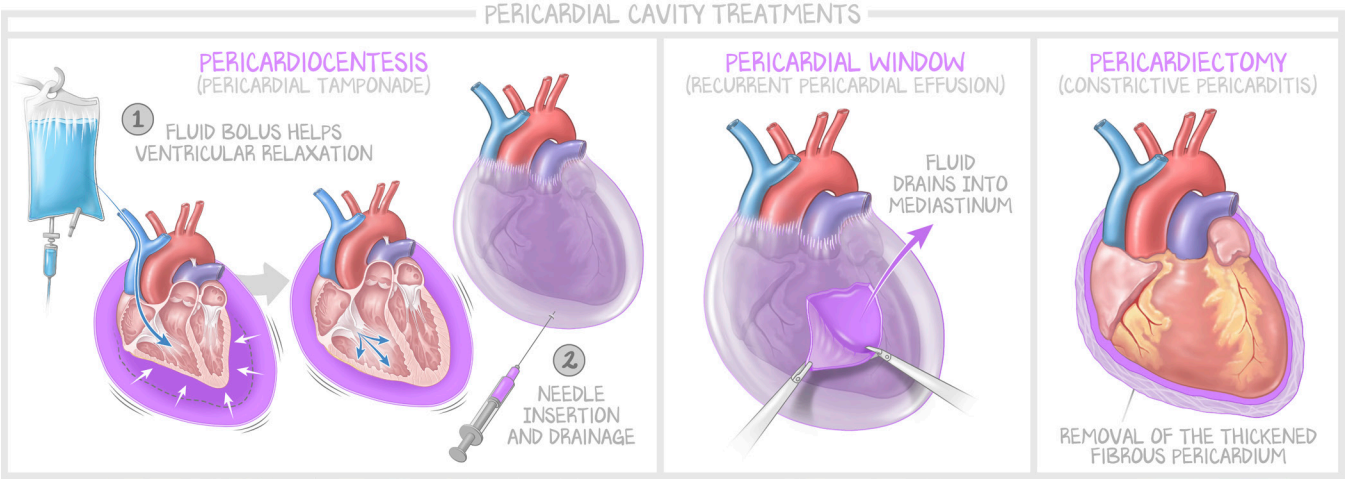

Figure 3.6: Pericardial Tamponade Treatment
If the diagnosis is tamponade, bolus a liter of saline or lactated ringers while you find the ultrasound and the pericardiocentesis needle. Immediate drainage is the only treatment for tamponade. Pericardial window, where an incision is made in the Pericardium, allows the drainage of fluid into the mediastinum, which has lymphatics to drain it. This is only useful for small recurrent effusions. Pericardiotomy is the removal of the Pericardium, which is done in constrictive pericarditis.

DIAGNOSIS	NOTES
Pericarditis	Inflammation of the Pericardium. Pleuritic chest pain that radiates to the back and improves with leaning forward. Pain can refer to the shoulder because of the phrenic nerve innervation. There will be a pericardial friction rub. It is usually viral, although there are many possible causes. Diagnosed by ECG showing global ST-segment elevations and PR-segment depressions. Treat with NSAIDs and colchicine . . . glucocorticoids if not able.
Pericardial effusion	A painless increase in the amount of fluid between the two layers of serous pericardium. Easily diagnosed by echocardiogram. Chest X-ray may show a bag-like enlarged shadow. Hemorrhagic effusion has lots of red cells. Suppurative effusion has pus, lots of white cells. Exudative effusions happen in heart failure and myxedema. Malignant effusion has blood and cancer cells.
Pericardial tamponade	A rapid or large rise in the amount of fluid (a super effusion) results in compression of the ventricles, preventing diastolic relaxation. Obstructive form of shock. Pulsus paradoxus, a drop in systolic BP by at least 10 mmHg, is sufficient to diagnose. Echocardiogram can guide pericardiocentesis.
Constrictive pericarditis	Long-term inflammation or recurrent acute pericarditis that causes thickening, scarring, and calcification of the epicardium. The serous pericardium becomes rigid like the fibrous pericardium. There is a pericardial knock, and the pericardium must be removed.

Table 3.1: Pericardial Disease in Review
High-yield points to remember.